Goal-directed therapy may improve outcome in complex patients – depending on the chosen treatment end point

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EDITORIAL

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Goal-directed therapy may improve outcome in complex patients – depending on the chosen treatment end point

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This editorial is related to the paper entitled "Goal-directed medical therapy and point of care testing improve outcomes after congenital heart surgery" by A.F. Rossi et al. (2005) 31:98–104

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One of the greatest opportunities to improve patient outcomes comes not from discovering new treatments, but using existing therapies more effectively [1]. Health services research is a relatively new academic discipline based on the study of methods of delivering healthcare safely, effectively, and efficiently. Emphasis is placed on systems and processes of healthcare delivery, on team performance, and on patient pathways and, above all, on patient outcome rather than on single interventions such as use of a new drug with narrowly defined endpoints. Health services research does fit comfortably alongside traditional academic science which many medical researchers see as occupying the high-ground of scientific discovery. Perhaps as a result of such perceptions, funding of health services research is minimal compared to the funding allocated to basic science and traditional clinical research [1]. However health services research has a particularly important role to play in ensuring cost-effective delivery of care in resource-limited healthcare systems. Inexpensive interventions can prove to be as effective if not more effective than some expensive or technically complex solutions. There is, however, a danger that commercial and academic vested interests continue to promote new products and innovations and their associated costly research programmes, whilst ignoring the benefits that might accrue from revisiting "old" therapies.

The quality of care delivery in an intensive care unit is governed by many factors. Units may set themselves (or have imposed upon them) standards which typically define required structural elements such as staffing levels and equipment provision. In addition, units may employ clinical guidelines or protocols to guide clinical interventions. Ultimately, patient outcome is influenced both by the system (designated by standards) and clinical interventions (therapies, protocols, guidelines). Health services research looks at systems or care in addition to the study intervention which would previously been the sole focus of much clinical research.

Guidelines define limits within which decisions can be made in the management of specific clinical problems and have been shown to improve outcome. Whilst guidelines permit doctors to operate within a range of acceptable practice, their aim is to guide, not to prohibit alternatives. A more proscriptive approach, that of protocol-directed therapy is often found in the ICU in the form of "goal-directed" therapeutic protocols. Such protocols typically mandate certain interventions when nodes in a treatment algorithm are reached, leaving the clinician with little room for alternative "off-protocol" care. Provided a relevant goal has been chosen and framed in a suitable evidence-based algorithm, goal-directed therapy has the potential to improve outcome as clinicians are constrained to offer therapy based on the "best practice" encapsulated in the protocol. For example, Rivers et al. studied adults admitted to an emergency department with severe sepsis or septic shock. The prompt institution of aggressive protocol-driven therapy aimed at achieving central venous oxygen saturations of greater than 70% improved survival in their controlled

study [2]. In mechanically ventilated adults with acute lung injury, restricting tidal volume to 6 ml per kilogram and plateau pressure to 30 cm of water or less, resulted in decreased mortality compared to traditional ventilation treatment [3]. In neonatology, a retrospective study showed impressively how preset arterial oxygen saturation goals may influence outcome [4]. Preterm babies given enough supplemental oxygen to maintain a pulse oximetry oxygen saturation of 70–90% had an improved outcome in the form of less retinopathy of prematurity, fewer ventilation days, and improved weight gain compared to babies whose treatment was directed to a "physiological" pulse oximeter oxygen saturation goal of 88–98%.

A pivotal issue in the success of any goal-directed therapy is the selection of the specific goal. Indicators used to achieve the desired therapeutic goal must, first, be easy and safe to obtain. Invasive techniques such as percutaneous insertion of pulmonary artery catheters may be judged to have an unfavourable risk/benefit ratio in children, despite their ability to provide information relevant to optimising cardiac output. Second, goals should be known to be associated with improved outcomes, not just assumed to be so. For instance a study of children with trauma and potential bleeding showed that the provision of aggressive blood pressure support may be detrimental [5]. Thus, blood pressure, although easily obtained and, at face value, a logical goal of resuscitative therapy, was not associated with improved outcome when used in this study. The impact of an intervention on a surrogate physiological endpoint such as blood pressure is insufficient evidence of clinical efficacy.

In this issue of the journal, Rossi and co-workers describe a significant lowering in mortality following cardiac surgical procedures coincident on the introduction of point of care measurement of blood lactate and the adoption of a management algorithm based on these measurements [6]. Lactate seems to be a good choice as an endpoint. Its measurement is easy, safe, and non-invasive and it correlates with outcome after paediatric cardiac surgery [7]. However, the inferences which can be drawn from the study of Rossi et al. [6] are, as the authors acknowledge, limited by its retrospective nature and the comparison of the interventional group with historical controls. The authors stress the stability of the surgical workforce but do not comment on the stability of cardiology, intensive care, and nursing teams. Changes in staff in these disciplines, and perhaps other unmeasured or unreported factors, might well have influenced morbidity and mortality. Even with a perfectly stable workforce, the uncontrolled design of the study does not allow us to be certain that lactate-driven therapy was the reason for the improved outcomes. Simply "protocolising" care without the introduction of any new intervention may improve outcomes as was shown by Morris et al. when comparing two therapeutic strategies for ARDS [8]. They concluded that the new treatment produced similar results to "standard" treatment, whilst noting that algorithm-derived standard treatment produced survival which was four times greater than that for "non-protocolised" historical controls.

In complex and high-risk situations such as paediatric cardiac intensive care, the use of evidence based clinical guidelines and associated goal-directed therapy has the potential to improve clinical outcomes. Intensivists should interpret reports such as that of Rossi et al. as supporting the logical concept of lactate-based goal-directed therapy but acknowledge that the true effect of this intervention can only be ascertained in a randomised-controlled trial. The intensive care community should strongly embrace health services research methods and lobby for funding of research of this type, seeking to achieve a cost-effective balance in the allocation of money to medical research and innovation.

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